UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/872,881	06/01/2001	Akira Suyama	14683	3628

7590 11/19/2002

Scully, Scott, Murphy & Presser
400 Garden City Plaza
Garden City, NY 11530-0299

EXAMINER
CHAKRABARTI, ARUN K

ART UNIT	PAPER NUMBER
1634	8

DATE MAILED: 11/19/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/872,881	Suyama
Examiner	**Art Unit**
Arun Chakrabarti	1634

-- **The MAILING DATE of this communication appears on the cover sheet with the correspondence address** --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on Oct 28, 2002 .

2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) 1-16 is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) 1-16 is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Specification

1. Claims 1,2, and 8-15 have been amended.

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CAR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

3. Claims 1-2 and 13-16 are rejected under 35 U.S.C. 103(a) over Carr (European patent Application, Publication NO: 0 246 864) (May 19, 1987) in view of Cantor et al. (U.S. Patent 6,007,987) (December 28, 1999).

Carr teaches a method of detecting or quantifying a target nucleic acid having a predetermined sequence in a specimen (Abstract) comprising:

a) preparing a probe A and a probe B (Abstract and Claim 1 and Example 1),

the probe A being a first probe which has a sequence F' complementary to a first partial sequence F of the target nucleic acid and a binding molecule bound to the sequence F' (Page 8, lines 41-42), and

the probe B being a second probe which has a sequence S' complementary to a second partial sequence S of the target nucleic acid (Page 6, lines 1-7);

b) hybridizing the first probe A with the first partial sequence F of the target nucleic acid and hybridizing the second probe B with the second partial sequence S of the target nucleic acid (Page 6, lines 1-7 and lines 30-32 and Claim 2);

c) ligating the first probe A and the second probe B both being hybridized with the target nucleic acid, thereby obtaining a probe (A+B) (Page 6, lines 30-33 and Claim 2 and Example 1);

d) binding the binding molecule to a substance capable of being paired up therewith, or by denaturing the hybridized complex thereby recovering the probe (A+B) (Page 6, lines 34-36 and 47-55 and Claim 7); and

e) recovering a single-stranded nucleic acid having the marker substance detected or identified, thereby detecting or quantifying the target nucleic acid in the specimen (Page 6, lines 13-23).

Carr teaches the amplification of the single-stranded nucleic acid present in a liquid phase by PCR, thereby performing an encode reaction (Page 6, lines 30-35 and Claim 4).

Carr does not teach a probe with a double-stranded flag containing 4 units consisting of SD, D0, D1 and ED each having an arbitrary sequence bound to each other sequentially in the order mentioned and a marker substance.

Cantor et al teach a probe with a double-stranded flag containing 4 units consisting of SD, D0, D1 and ED each having an arbitrary sequence bound to each other sequentially in the order mentioned and a marker substance (Column 4, lines 9-17 and Column 7, lines 9-34 and column 9, lines 11-25).

Carr does not teach the multiplexing of detecting or quantifying a target nucleic acid having a predetermined sequence in a specimen with multiple probes A1-An and B1-Bn.

Cantor et al teach the multiplexing of detecting or quantifying a target nucleic acid having a predetermined sequence in a specimen with multiple probes A1-An and B1-Bn (Column 4, lines 9-17 and Column 7, lines 9-34 and column 9, line 11 to Column 10, line 52).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to substitute and combine a probe with a double-stranded flag containing 4 units consisting of SD, D0, D1 and ED and the multiplexing of detecting or quantifying a target nucleic acid having a predetermined sequence in a specimen with multiple probes A1-An and B1-Bn of Cantor et al. into the method of detecting or quantifying a target nucleic acid having a predetermined sequence in a specimen of Carr, since Cantor et al state, "These arrays may be

bound to solid supports and are useful for determining the nucleotide sequence of unknown nucleic acids and for the detection, identification and purification of target nucleic acids in biological samples (Column 4, lines 13-16)". Moreover, Cantor et al. state, "A principal advantage of this probe is in its structure. Hybridization of the target nucleic acid is encouraged due to its favorable thermodynamic conditions established by the presence of the adjacent double-strandedness of the probe (Column 7, lines 29-33)". By employing scientific reasoning, an ordinary artisan would have substituted and combined a probe with a double-stranded flag containing 4 units consisting of SD, D0, D1 and ED and the multiplexing of detecting or quantifying a target nucleic acid having a predetermined sequence in a specimen with multiple probes A1-An and B1-Bn of Cantor et al. into the method of detecting or quantifying a target nucleic acid having a predetermined sequence in a specimen of Carr in order to improve the detection and identification of multiple target nucleic acids. An ordinary practitioner would have been motivated to combine and substitute a probe with a double-stranded flag containing 4 units consisting of SD, D0, D1 and ED and the multiplexing of detecting or quantifying a target nucleic acid having a predetermined sequence in a specimen with multiple probes A1-An and B1-Bn of Cantor et al. into the method of detecting or quantifying a target nucleic acid having a predetermined sequence in a specimen of Carr, in order to achieve the express advantages noted by Cantor et al., of the structure of probes which provides hybridization of the target nucleic acid encouraged due to its favorable thermodynamic conditions established by the presence of the adjacent double-strandedness of the probe and also to achieve the express advantages of arrays of

probes which are useful for determining the nucleotide sequence of unknown nucleic acids and for the detection, identification and purification of target nucleic acids in biological samples.

4. Claims 1-9 and 13-16 are rejected under 35 U.S.C. 103(a) over Carr (European patent Application, Publication NO: 0 246 864) (May 19, 1987) in view of Cantor et al. (U.S. Patent 6,007,987) (December 28, 1999) further in view of Wong (U.S. Patent 5,935,793) (August 10, 1999).

Carr in view of Cantor et al teach the method of claims 1-2 and 13-16 as described above.

Carr in view of Cantor et al do not teach the hybridization of the tag sequence Tg with a complementary sequence tag Tg' to recover the probes.

Wong teaches the hybridization of the tag sequence Tg with a complementary sequence tag Tg' (Example 2, Column 24, lines 24-30).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to substitute and combine the hybridization of the tag sequence Tg with a complementary sequence tag Tg' of Wong into the method of detecting or quantifying a target nucleic acid having a predetermined sequence in a specimen of Carr in view of Cantor et al., since Wong states, "This results in an increased quantity of identifier tag with a relative reduction in sample-derived background, so that sensitivity for detecting the identifier tag on a probe-array can be substantially increased (Column 10, lines 19-22)". By employing scientific reasoning, an ordinary artisan would have substituted and combined the hybridization of the tag sequence Tg with a complementary sequence tag Tg' of Wong into the method of detecting or quantifying a

target nucleic acid having a predetermined sequence in a specimen of Carr in view of Cantor et al. in order to improve the detection and identification of multiple target nucleic acids. An ordinary practitioner would have been motivated to combine and substitute the hybridization of the tag sequence Tg with a complementary sequence tag Tg' of Wong into the method of detecting or quantifying a target nucleic acid having a predetermined sequence in a specimen of Carr in view of Cantor et al. in order to achieve the express advantages noted by Wong, of a method that results in an increased quantity of identifier tag with a relative reduction in sample-derived background, so that sensitivity for detecting the identifier tag on a probe-array can be substantially increased.

5. Claims 1-2 and 10-16 are rejected under 35 U.S.C. 103(a) over Carr (European patent Application, Publication NO: 0 246 864) (May 19, 1987) in view of Cantor et al. (U.S. Patent 6,007,987) (December 28, 1999) further in view of Cleuziat et al. (U.S. Patent 6,218,151 B1) (April 17, 2001).

Carr in view of Cantor et al teach the method of claims 1-2 and 13-16 as described above.

Carr in view of Cantor et al do not teach the sequencing by transcription of a single stranded nucleic acid by use of two primers.

Cleuziat et al. teach the sequencing by transcription of a single stranded nucleic acid by use of two primers. (Figure 13 and Column 29, line 39 to Column 30, line 6).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to substitute and combine the sequencing by transcription of a single

stranded nucleic acid by use of two primers. of Cleuziat et al. into the method of detecting or quantifying a target nucleic acid having a predetermined sequence in a specimen of Carr in view of Cantor et al., since Cleuziat et al state, "The method is therefore composed of a single stage, without subsequent or intermediate addition of reagents, or the use of enzymatic activity, in particular nuclease activity (Column 30, lines 3-5)". By employing scientific reasoning, an ordinary artisan would have substituted and combined the sequencing by transcription of a single stranded nucleic acid by use of two primers. of Cleuziat et al. into the method of detecting or quantifying a target nucleic acid having a predetermined sequence in a specimen of Carr in view of Cantor et al., in order to improve the detection and identification of nucleic acids. An ordinary practitioner would have been motivated to combine and substitute the sequencing by transcription of a single stranded nucleic acid by use of two primers. of Cleuziat et al. into the method of detecting or quantifying a target nucleic acid having a predetermined sequence in a specimen of Carr in view of Cantor et al., in order to achieve the express advantages noted by Cleuziat et al., of the method composed of a single stage, without subsequent or intermediate addition of reagents, or the use of enzymatic activity, in particular nuclease activity.

Response to Amendment

6. In response to amendment, all 112 (second paragraph) rejections are hereby withdrawn. However, all 103(a) rejections have been properly maintained.

Response to Arguments

7. Applicant's arguments filed on October 28, 2002 have been fully considered but they are not persuasive.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Applicant argues that there is no motivation to combine the references. This argument is not persuasive especially in the presence of strong motivation provided by Cantor et al. since Cantor et al state, "These arrays may be bound to solid supports and are useful for determining the nucleotide sequence of unknown nucleic acids and for the detection, identification and purification of target nucleic acids in biological samples (Column 4, lines 13-16)". Same logic is applicable to the motivations of combining other references.

Applicant argues that present invention does not require any step of distinguishing tags by length which is carried out by Wong reference. This argument is not persuasive especially in the presence of "comprising" language of the claims. "Comprising" language allows any intermediate or additional step to be included in the claim. Same logic is applicable to the argument raised against rejection based on Cleuziat et al reference.

Applicant argues that Cantor reference does not teach the double stranded flag containing 4 units of the claimed invention. Applicant argues that the word "flag containing 4 units" was not

found in Cantor reference and only the word "single stranded" or "fixed to an array" are found. Applicant argues that because Cantor has a preferred embodiment of array hybridization, Cantor is limited to the preferred embodiment. This argument is not persuasive. As MPEP 2123 states "Disclosed examples and preferred embodiments do not constitute a teaching away from a broader disclosure or nonpreferred embodiments. In re Susi,169 USPQ 423 (CCPA 1971)." MPEP 2123 also states " A reference may be relied upon for all that it would have reasonably suggested to one having ordinary skill the art, including nonpreferred embodiments. Merck & Co. v. Biocraft Laboratories , 10 USPQ2d 1843 (Fed. Cir. 1989)." It is clear that simply because Cantor has a preferred embodiment, this embodiment does not prevent the reference from suggesting broader embodiments in the disclosure and that this does not constitute a teaching away. Although Cantor reference uses arrays for hybridization, the property of double stranded flag containing 4 units is inherently present in this chemically and structurally identical molecule. For example, Cantor teaches, "Arrays comprise 4R different probes representing every member of the random sequence" (Column 13, lines 6-7). Moreover, MPEP 2111 states, "Claims must be given their broadest reasonable interpretation. During patent examination, the pending claims must be "given the broadest reasonable interpretation consistent with the specification". Applicant always has the opportunity to amend the claims during prosecution and broad interpretation by the examiner reduces the possibility that the claim, once issued, will be interpreted more broadly than it is justified. *In re Prater,* 415 F.2d 1393, 1404-05, 162 USPQ

541, 550-51 (CCPA 1969)". In this case, 4R different probes of Cantor can be considered as double stranded flag containing 4 units.

Therefore, all the 103 (a) rejections made in the first office action are hereby properly maintained.

Conclusion

8. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CAR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CAR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Arun Chakrabarti, Ph.D. whose telephone number is (703) 306-5818. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached on (703) 308-1152.Any inquiry of a general nature or relating to the status

of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196. Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission via the P.T.O. Fax Center located in Crystal Mall 1. The CM1 Fax Center numbers for Technology Center 1600 are either (703) 305-3014 or (703) 308-4242. Please note that the faxing of such papers must conform with the Notice to Comply published in the Official Gazette, 1096 OG 30 (November 15, 1989).

Arun Chakrabarti
Patent Examiner
Art Unit 1634

November 6, 2002

W. Gary Jones
Supervisory Patent Examiner
Technology Center 1600